

TENT COOPERATION TREA 7

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

BAYER AKTIENGESELLSCHAFT
D-51368 Leverkusen
ALLEMAGNEDate of mailing (day/month/year)
27 août 2001 (27.08.01)Applicant's or agent's file reference
Le A 33 162-WO Hb

IMPORTANT NOTIFICATION

International application No.
PCT/EP99/10110International filing date (day/month/year)
20 décembre 1999 (20.12.99)

1. The following indications appeared on record concerning:

☒ the applicant ☒ the inventor ☐ the agent ☐ the common representative

Name and Address

FITZGERALD, Mary, F.
2 Paternoster Court
Cassington Road
Yarnton, Oxon OX5 1QB
United Kingdom

State of Nationality

GB

State of Residence

GB

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☐ the name ☒ the address ☐ the nationality ☐ the residence

Name and Address

FITZGERALD, Mary, F.
2 Paternoster Court
Cassington Road
Yarnton, Oxon OX5 1QB
United Kingdom

State of Nationality

GB

State of Residence

GB

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned
☐ the International Searching Authority ☒ the elected Offices concerned
☐ the International Preliminary Examining Authority ☐ other:The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

Jean-Marie MCADAMS

Facsimile No.: (41-22) 740.14.35

Telephone No.: (41-22) 338.83.38

Copy for the designated Office (DO/US)

PCT COOPERATION TRE/

PCT

NOTIFICATION RELATING TO PRIORITY CLAIM

(PCT Rules 26bis.1 and 26bis.2 and
Administrative Instructions, Sections 402 and 409)

From the INTERNATIONAL BUREAU

To:

BAYER AKTIENGESELLSCHAFT
D-51368 Leverkusen
ALLEMAGNE

Date of mailing (day/month/year) 03 March 2000 (03.03.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference Le A 33 162-WO Hb	
International application No. PCT/EP99/10110	International filing date (day/month/year) 20 December 1999 (20.12.99)
Applicant BAYER AKTIENGESELLSCHAFT et al	

The applicant is hereby **notified** of the following in respect of the priority claim(s) made in the international application.

1. ☒ **Correction of priority claim.** In accordance with the applicant's notice received on: 28 February 2000 (28.02.00), the following priority claim has been corrected to read as follows:

GB 24 September 1999 (24.09.99) 9922709.2

- ☐ even though the indication of the number of the earlier application is missing.
☐ even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document:

2. ☐ **Addition of priority claim.** In accordance with the applicant's notice received on: , the following priority claim has been added:

- ☐ even though the indication of the number of the earlier application is missing.
☐ even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document:

3. ☐ As a result of the correction and/or addition of (a) priority claim(s) under items 1 and/or 2, the (earliest) priority date is:

4. ☐ **Priority claim considered not to have been made.**

- ☐ The applicant failed to respond to the invitation under Rule 26bis.2(a) (Form PCT/IB/316) within the prescribed time limit.
☐ The applicant's notice was received after the expiration of the prescribed time limit under Rule 26bis.1(a).
☐ The applicant's notice failed to correct the priority claim so as to comply with the requirements of Rule 4.10.
The applicant may, before the technical preparations for international publication have been completed and subject to the payment of a fee, request the International Bureau to publish, together with the international application, information concerning the priority claim. See Rule 26bis.2(c) and the PCT Applicant's Guide, Volume I, Annex B2(II).

5. ☐ In case where multiple priorities have been claimed, the above item(s) relate to the following priority claim(s):

6. A copy of this notification has been sent to the receiving Office and
☒ to the International Searching Authority (where the international search report has not yet been issued).
☒ the designated Offices (which have already been notified of the receipt of the record copy).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Form PCT/IB/318 (July 1998)

Authorized officer

S. De Michiel

Telephone No. (41-22) 338.83.38

0031443

BEST AVAILABLE COPY

PCT COOPERATION TREATY

PCT

NOTIFICATION RELATING TO PRIORITY CLAIM

(PCT Rules 26bis.1 and 26bis.2 and
Administrative Instructions, Sections 402 and 409)

From the INTERNATIONAL BUREAU

To:

BAYER AKTIENGESELLSCHAFT
D-51368 Leverkusen
ALLEMAGNE

Date of mailing (day/month/year) 03 March 2000 (03.03.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference Le A 33 162-WO Hb	
International application No. PCT/EP99/10110	International filing date (day/month/year) 20 December 1999 (20.12.99)
Applicant BAYER AKTIENGESELLSCHAFT et al	

The applicant is hereby **notified** of the following in respect of the priority claim(s) made in the international application.

1. ☒ **Correction of priority claim.** In accordance with the applicant's notice received on: 28 February 2000 (28.02.00), the following priority claim has been corrected to read as follows:

GB 30 December 1998 (30.12.98) 9828845.9

- ☐ even though the indication of the number of the earlier application is missing.
☐ even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document:

2. ☐ **Addition of priority claim.** In accordance with the applicant's notice received on: , the following priority claim has been added:

- ☐ even though the indication of the number of the earlier application is missing.
☐ even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document:

3. ☐ As a **result of the correction and/or addition** of (a) priority claim(s) under items 1 and/or 2, the (earliest) priority date is:

4. ☐ **Priority claim considered not to have been made.**

- ☐ The applicant failed to respond to the Invitation under Rule 26bis.2(a) (Form PCT/IB/316) within the prescribed time limit.
☐ The applicant's notice was received after the expiration of the prescribed time limit under Rule 26bis.1(a).
☐ The applicant's notice failed to correct the priority claim so as to comply with the requirements of Rule 4.10.

The applicant may, before the technical preparations for international publication have been completed and subject to the payment of a fee, request the International Bureau to publish, together with the international application, information concerning the priority claim. See Rule 26bis.2(c) and the PCT Applicant's Guide, Volume I, Annex B2(1B).

5. ☐ In case where **multiple priorities** have been claimed, the above item(s) relate to the following priority claim(s):

6. A copy of this notification has been sent to the receiving Office and

- ☒ to the International Searching Authority (where the international search report has not yet been issued).
☒ the designated Offices (which have already been notified of the receipt of the record copy).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. (41-22) 740.14.35	Authorized officer S. De Michiel Telephone No. (41-22) 338.83.38
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F ENT COOPERATION TREA

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

BAYER AKTIENGESELLSCHAFT
D-51368 Leverkusen
ALLEMAGNE

Date of mailing (day/month/year) 05 April 2001 (05.04.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference Le A 33 162-WO Hb	
International application No. PCT/EP99/10110	International filing date (day/month/year) 20 December 1999 (20.12.99)

1. The following indications appeared on record concerning:

☒ the applicant ☒ the inventor ☐ the agent ☐ the common representative

Name and Address	State of Nationality DE	State of Residence DE
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☒ the person ☒ the name ☒ the address ☒ the nationality ☒ the residence

Name and Address MAYR, Lorenz Sternstrasse 40 D-42799 Leichlingen Germany	State of Nationality DE	State of Residence DE
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:

Please note that the above-mentioned person has been added into our records as applicant/inventor for US only.

4. A copy of this notification has been sent to:

<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer A. Karkachi Telephone No.: (41-22) 338.83.38
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PCT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C. 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 14 August 2000 (14.08.00)	Applicant's or agent's file reference Le A 33 162-WO Hb
International application No. PCT/EP 99/10110	Priority date (day/month/year) 30 December 1998 (30.12.98)
International filing date (day/month/year) 20 December 1999 (20.12.99)	
Applicant FITZGERALD, Mary, F. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

05 July 2000 (05.07.00)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Charlotte ENGER

Telephone No.: (41-22) 338.83.38

PCT

REC'D 05 APR 2001

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

14

Applicant's or agent's file reference Le A 33 162-WO Hb	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP99/10110	International filing date (day/month/year) 20/12/1999	Priority date (day/month/year) 30/12/1998
International Patent Classification (IPC) or national classification and IPC C07C59/88		
Applicant BAYER AKTIENGESELLSCHAFT et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.


2. This REPORT consists of a total of 7 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 05/07/2000	Date of completion of this report 02.04.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Villa Riva, A Telephone No. +49 89 2399 8404



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/10110

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-109 as originally filed

Claims, No.:

1-17 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/10110

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-5 (N,IS,IA), 13 (IA).

because:

☒ the said international application, or the said claims Nos. 13 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-5.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	6-11
	No:	Claims	12,13
Inventive step (IS)	Yes:	Claims	
	No:	Claims	6-17
Industrial applicability (IA)	Yes:	Claims	6-12,14-17

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/10110

No: Claims

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Section III

Claim 13 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT).

Section V

1. Reference is made to the following documents:

D1: WO 96 15 096 A

D2: WO 97 43 247 A

D3: WO 98 09 940 A

D4: WO 98 22 436 A

D5: BARNES P J: Trends in Pharmacological Sciences, GB, Elsevier Trends Journal, Cambridge, vol. 19, no. 10, 1998 (1998-10), pages 415-423.

D6: WEHR A: 'Proteasehemmer-nicht nur bei AIDS wirksam.' Deutsche Medizinische Wochenschrift, vol. 123, no. 1-2, 1998, pages a9-10.

D7: RICOU B ET AL: 'Matrix Metalloproteinases and TIMP in Acute Respiratory Distress Syndrome' Am J Respir Crit Care Med, vol. 154, 1996, pages 346-352.

Unless otherwise indicated, reference is made to the relevant passages emphasized in the International Search Report.

2. Novelty (PCT Art. 33(1) and (2))

Several biarylbutyric, -hydroxybutyric and -pentanoic acid derivatives are known for their MMP (matrix metalloproteinase) inhibiting activity (see e.g. D2-D4). In particular D1 discloses the activity of compounds which fall under the general formula (I') of present claim 9 as inhibitors of MMPs, and in particular also the compound in claim 11 (see Table XX in D2 (the compound in claim 10 is disclosed as a racemate only). Therefore, the subject-matter of present claims 12 and 13 does not appear to be novel.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP99/10110

3. Inventive Step (PCT Art. 33(1) and (3))

D1 discloses the fact that several of the compounds listed in present claim 6, 9 and 11 are inhibitors of MMP enzymes. The technical problem can be seen as to provide the use of MMP inhibitors against respiratory diseases. However, D5-D7 disclose the links which exist between the activity of these enzymes and some respiratory and inflammatory diseases. Therefore, it would be obvious to the skilled person to try compounds, which are known as MMP inhibitors, in the preparation of medicaments against said diseases. This affects the inventivity of present claims 6, 9-11, 14-17. As far as the new compounds in claims 7, 8 are concerned, the technical problem has to be rephrased as to obtain alternative biarylbutyric acid derivatives intended to be used as MMP inhibitors.

In this context, the simple resolution of the racemate into enantiomers, as it is performed for the 4'-ethoxy and the 4'-chlorine isoindol derivative cannot be considered inventive. Indeed, if a racemate is known to have pharmacological properties (as it appears from D1 in the case of these two compounds), it would be obvious to the skilled person to isolate the pure single optical isomers and test them in the same pharmacological context, in order to reduce the dosage or the side effects, or to obtain a more specific action. In addition, for the 4'-chlorine compound, the separation of the enantiomers is already hinted at in D1, Table XX.

Since it is not predictable which biological effect will be brought about by a chemical change, the chemical modifications which give rise to the other compounds in present claim 7 could account for the presence of an inventive step if any technical effect could be shown for them, which is not the case (see remarks on Art. 5 and 6 PCT below).

4. Industrial Applicability (PCT Art. 33(1) and (4))

For the assessment of the present claim 13 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound

for the manufacture of a medicament for a new medical treatment.

Section VI

5. The potentially relevant intermediate document WO 99 18079 A, published on 15 April 1999 (filing date 23.9.98, priority date 7.6.95, publication date 6.10.97) is quoted according to Rules 70.10 and 64.3 PCT.

Section VIII

6. The fact that the compounds of the present application can be used for the preparation of medicaments against respiratory diseases does not appear to be sufficiently supported (contrary to Art. 5 PCT) by the present specification. Indeed, it is only shown for 5 compounds that they are able to inhibit MMP-12 (table 3), and for other 2 selectivity data are provided (table 4). However, in the title to table 3 MMP-13 is mentioned. In table 4 a mixture of IC_{50} and K_i data are given. This lack of precision renders the data so unclear, contrary to Art. 6 PCT, that it appears to be impossible to establish whether the technical problem has been solved at all.

P NT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference Le A 33 16-WO Ho	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 99/ 10110	International filing date (day/month/year) 20/12/1999	(Earliest) Priority Date (day/month/year) 30/12/1998
Applicant BAYER AKTIENGESELLSCHAFT et al		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.



Certain claims were found unsearchable (See Box I).

3.



Unity of invention is lacking (see Box II).

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures.

INTERNATIONAL SEARCH REPORT

national application No.
PCT/EP 99/10110

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 1-5
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-5

Present claims 1-5 relate to the use of an extremely large number of possible compounds for the preparation of medicaments against respiratory diseases. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for the use of a very small proportion of the compounds among those listed in the claims 1-5 only. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for the claims which appear to be supported and disclosed, namely claims 6-17.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

National Application No

PCT/EP 99/10110

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07C59/88 C07C59/48 C07C59/68 C07D317/46 C07D253/08
 A61K31/40 A61K31/53 A61P11/00 A61P29/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07C C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 99 18079 A (PURCHASE CLAUDE FORSEY JR ;WARNER LAMBERT CO (US); ROTH BRUCE DAVI) 15 April 1999 (1999-04-15) abstract page 9, line 3-14 formula I	12, 13
X	WO 96 15096 A (SCHNEIDER STEPHAN ;BENZ GUENTER H H H (DE); DIXON BRIAN RICHARD (U) 23 May 1996 (1996-05-23)	12, 13
Y	page 7, line 1 -page 11, line 6 examples tables, particularly tables XX, XXV --- -/-	6-11, 14-17



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

26 April 2000

Date of mailing of the international search report

18. 05. 00

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 99/10110

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